

FOOD AND DRUG ADMINISTRATION (FDA)
Center for Drug Evaluation and Research (CDER)

Peripheral and Central Nervous System Drugs Advisory Committee (PCNS) Meeting
FDA White Oak Campus, Building 31 Conference Center, the Great Room (Rm. 1503)
10903 New Hampshire Avenue, Silver Spring, Maryland
November 24, 2015

DRAFT QUESTIONS

1. **DISCUSSION:** Discuss the strength of efficacy evidence provided by Study 1 with particular consideration of the following issues and any other issues that you think may be important:
 - a. Discrepant results of the two dosing regimens despite similar exposure to drisapersen
 - b. Lack of statistically significant results on secondary endpoints
2. **VOTE:** What overall impact do the issues discussed in question #1 have on the persuasiveness of Study 1?
 - a. Strengthen
 - b. Weaken
 - c. No effect
3. **DISCUSSION:** Discuss the strength of efficacy evidence provided by Study 2 with particular consideration of the following issues and any other issues that you think may be important:
 - a. Lack of statistical significance of the primary outcome measure ($p = 0.07$ on ITT analysis, $p = 0.23$ on per protocol analysis)
 - b. 3 mg/kg group numerically inferior to placebo
 - c. 6 mg/kg group numerically inferior to placebo for most secondary endpoints
4. **VOTE:** What overall impact do the issues discussed in question #2 have on the persuasiveness of Study 2?
 - a. Strengthen
 - b. Weaken
 - c. No effect
5. **DISCUSSION:** Discuss the evidence provided by Study 3 with particular consideration of the following issues and any other issues that you think may be important:
 - a. Lack of statistical significance of the primary outcome measure ($p = 0.42$) in a well-powered Phase 3 study
 - b. Lack of nominally statistically significant results on all secondary endpoints
6. **VOTE:** What is the impact of Study 3 results on the persuasiveness of findings in Study 1 and Study 2?
 - a. Strengthen
 - b. Weaken
 - c. No effect

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DRAFT QUESTIONS (cont.)

7. **DISCUSSION:** Drisapersen was designed to increase production of dystrophin. Discuss the evidence presented about dystrophin production, including the following:
- a. Similar number of patients with skipped band of mRNA detected by PCR in the placebo group and drisapersen group
 - b. Similar number of patients with dystrophin increase from baseline in the placebo group and drisapersen group on immunofluorescence testing
 - c. Lack of notable increase in dystrophin with drisapersen treatment on western blot analysis (pre-treatment levels <1% and post-treatment levels <1%)
8. **VOTE:** What is the impact of the dystrophin results on the interpretation of the clinical results?
- a. Strengthen
 - b. Weaken
 - c. No effect